

IN THE CLAIMS:

A marked up version of the claims showing the amendments is attached hereto as Exhibit A. Matter that has been deleted from claims 1, 6, 30, 44, 50, 72-74, 76, 100 and 105 is indicated by brackets and matter that has been added is indicated by underlining. A clean version of the pending claims, as amended, is attached hereto as Exhibit B.

Please amend the claims as follows:

Please ~~cancel~~ claims 101-104 without prejudice.

Please amend claims 1, 6, 30, 44, 50, 72-74, 76, 100 and 105 to read as follows:

1. (Four Times Amended) A method of determining a consensus profile for a first plurality of drug perturbations to a cell type or organism, said method comprising identifying among a plurality of sets of cellular constituents in a plurality of response profiles one or more sets of cellular constituents, each of said one or more sets of cellular constituents being upregulated or downregulated by said first plurality of drug perturbations, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different drug perturbation to said type of cell or organism, wherein each set of cellular constituents in said plurality of sets of cellular constituents consists of cellular constituents that co-vary under a second plurality of perturbations or that are co-regulated, wherein said plurality of response profiles comprises at least five response profiles, and wherein said consensus profile for said first plurality of drug perturbations comprises measurements of said one or more sets of cellular constituents.

6. (Three Times Amended) The method of claim 1, wherein said first plurality of drug perturbations is associated with a particular biological effect.

30. (Three Times Amended) The method of claim 1 wherein the consensus profile is the intersection of the sets of cellular constituents activated or de-activated by said first plurality of drug perturbations.

44. (Four Times Amended) A method for grouping measured response profiles in sets which are associated with similar biological effects comprising grouping response profiles among a plurality of response profiles into sets, each of said sets of response profiles consisting of response profiles in which the responses of one or more sets of genes in each

response profile are similar among response profiles in the set, each response profile in said plurality of response profiles (i) comprising measurements of transcript levels of a plurality of genes, and (ii) resulting from a different perturbation, wherein each of said sets of genes consists of genes that co-vary under a plurality of perturbations or that are co-regulated, wherein said plurality of response profiles comprises at least five response profiles.

50. (Amended) The method of claim 49, wherein the objective statistical test comprises:

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Etc
- (a) determining an actual fractional improvement in the cluster analysis of the response profiles;
  - (b) generating permuted response profiles by means of Monte Carlo randomization of gene index for each response profile across the measured genes;
  - (c) performing cluster analysis on the permuted response profiles;
  - (d) determining the fractional improvement in the cluster analysis of the permuted response profiles; and
  - (e) repeating said steps of generating permuted response profiles and performing cluster analysis on the permuted response profiles so that a distribution of fractional improvements is obtained;

wherein the statistical significance is determined by comparing the actual fractional improvement to the distribution of fractional improvements.

72. (Three Times Amended) A method for analyzing response data from a biological sample comprising

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- (a) grouping cellular constituents from the biological sample into sets of genes that co-vary in a plurality of response profiles, each response profile in said plurality of response profiles (i) comprising measurements of transcript levels of a plurality of genes, and (ii) resulting from a different perturbation to said biological sample; and
  - (b) grouping the plurality of response profiles into sets of response profiles that similarly affect genes,

wherein said plurality of response profiles comprises at least five response profiles.

73. (Amended) The method of claim 72, wherein one or more genes which co-vary in association with a particular biological effect are identified from the sets of genes that co-vary in said plurality of response profiles.

74. (Amended) The method of claim 72, wherein one or more response profiles that are associated with a particular biological effect are identified from the sets of response profiles that similarly affect genes.

76. (Amended) The method of claim 73, wherein one or more genes associated with said biological effect are identified.

100. (Three Times Amended) A method of grouping sets of drug perturbations that similarly affect cellular constituents in a cell type or organism among a plurality of drug perturbations comprising grouping response profiles among a plurality of response profiles in sets, each of said sets of response profiles consisting of response profiles in which the responses of one or more sets of cellular constituents are similar among the response profiles in the set, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different drug perturbation, wherein each of said sets of cellular constituents consists of cellular constituents that co-vary under a plurality of perturbations or that are co-regulated, thereby grouping said sets of drug perturbations, wherein said plurality of response profiles comprises at least five response profiles.

105. (Amended) A method for grouping measured response profiles in sets which are associated with similar biological effects comprising grouping response profiles in sets among a plurality of response profiles by cluster analysis of said plurality of response profiles, said sets of response profiles consisting of response profiles having similar responses of a group of cellular constituents, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different perturbation, wherein a statistical significance for the sets of response profiles is determined by means of an objective statistical test.

Please add the following new claims:

107. (New) The method of claim 38, wherein the plurality of response profiles comprises more than five response profiles.

108. (New) The method of claim 107, wherein the plurality of response profiles comprises more than ten response profiles.

109. (New) The method of claim 108, wherein the plurality of response profiles comprises more than 50 response profiles.

110. (New) The method of claim 109, wherein the plurality of response profiles comprises more than 100 response profiles.

111. (New) The method of claim 38, wherein said first plurality of perturbations is associated with a particular biological effect.

112. (New) The method of claim 111, wherein the particular biological effect is the effect of a particular class or type of drug.

113. (New) The method of claim 111, wherein the particular biological effect is a therapeutic effect.

114. (New) The method of claim 111, wherein the particular biological effect is a toxic effect.

115. (New) The method of claim 38, wherein each of the sets of genes consists of genes which are co-regulated.

116. (New) The method of claim 38, wherein each of the sets of genes consists of genes which co-vary in the plurality of response profiles.

117. (New) The method of claim 116, wherein the genes which co-vary are identified by cluster analysis of genes in the plurality of response profiles.

118. (New) The method of claim 117, wherein the cluster analysis is done by means of a clustering algorithm.

119. (New) The method of claim 118, wherein the clustering algorithm is *hclust*.

120. (New) The method of claim 117, wherein said cluster analysis determines a clustering tree, the genes which co-vary comprising branches of said clustering tree.

121. (New) The method of claim 120, wherein the sets of co-varying genes are selected from a branching level of the clustering tree.

122. (New) The method of claim 117, wherein a statistical significance for the sets of co-varying genes is determined by means of an objective statistical test.

123. (New) The method of claim 122, wherein the objective statistical test comprises:

- (a) determining an actual fractional improvement in cluster analysis of the genes;
- (b) generating permuted response of genes by means of Monte Carlo randomization of perturbation index for the response of each gene across all perturbations;
- (c) performing cluster analysis on the permuted response of genes;
- (d) determining the fractional improvement in the cluster analysis on the permuted response of genes; and
- (e) repeating said steps of generating permuted response of genes and performing cluster analysis on the permuted response of genes so that a distribution of fractional improvements is obtained;

wherein the statistical significance is determined by comparing the actual fractional improvement to the distribution of fractional improvements.